UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,714	02/17/2006	Atsushi Ochiai	00005001287	3272

5514 7590 01/03/2008

FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
01/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,714	OCHIAI ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 17 February 2006 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2/17/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4 are pending.

Information Disclosure Statement

The IDS filed 2/17/06 has been considered and an initialed copy of the PTO-1449 is enclosed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. In claim 2(a) it is not clear if the antibody binds IGF-I and IGF-II at the same time or if the antibody can bind IGF-I and IGF-II but binds them separately.

b. In claim 2, it is not clear what the difference is between 2(b) and 2(c). The composition in each case comprises the same components. It appears from the specification that applicant intends 2(c) to be a packaging (see [0061]). If applicant re-writes this claim applicant is cautioned against the addition of new matter into the claim.

c. In claim 2(e) it is not clear what applicant means by the "other molecules" because first there is improper antecedent basis for this terminology and second, what are "other molecules"?

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing an antibody and fragments thereof, single-chain Fv (scFv), dsFv and diabodies wherein they comprise 6 CDRs, three from the VH domain and three from the VL domain, does not reasonably provide enablement for a substance or a CDR-containing peptide that does not contain a full set of 6 CDRs from the VH and the VL domains as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

With respect to a CDR-containing peptide, the following applies:

The claim is broadly drawn to a method of producing a CDR-containing peptide which does not contain the full set of 6 CDRs and would not bind antigen.

The specification discloses only a monoclonal antibody (KM1468) that contains both a VH and a VL chain. The specification does not enable a CDR-containing peptide which does not contain 6 CDRs and bind antigen.

The claims encompass methods of producing a humanized antibody, a humanized scFv and fragments thereof, which do not contain a full set of 6 CDRs and do not bind antigen or the same antigen as the parental non-human antibody and can

retain a/some murine residue(s) in the framework regions (i.e., substantially identical to human framework regions). It is well established in the art that the formation of an intact antigen-binding site of all antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope (Paul, Fundamental Immunology, 3rd Edition, 1993, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions"). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites (Paul, page 293, first column, lines 3-8 and line 31 to column 2, line 9 and lines 27-30). Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al(Proc. Natl. Acad. Sci. USA 1982 Vol. 79: page 1979). Rudikoff et al teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that the CDR-containing peptide as defined by the claims, which may contain less than the full complement of CDRs from the heavy and light chain variable regions have the required

binding function. Applicants have provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability of producing a CDR-containing peptide containing fewer than 6 CDRs.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to a method of producing a CDR-containing peptide. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

With respect to "substance" the following applies:

The claims are directed to any substance which inhibits the activity of IGF-I and IGF-II. 'Substance' reads on oligonucleotides, DNA sequences, organic compounds (small and large), peptides, polypeptides, antisense, etc. Thus, the terminology "substance" reads on a vast multitude of compounds.

In support of the breadth of this claim, applicant has only demonstrated an antibody. Applicant has not provided a core structure or sequence that is needed for the organic compound or nucleic acid or amino acid sequences that is needed for the inhibition of IGF-I and IGF-II activity. Absent this core structure or sequence (ie guidance), one skilled in the art would have to sort through the vast multitudes of compounds to determine which compounds have the claimed ability. Thus, one skilled in the art would have to under go undue experimentation to make the claimed inveniton.

Requirement for Information

Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application.

In response to this requirement, please provide answers to each of the following interrogatories eliciting factual information:

In pages 16-17 of the specification, applicant refers to antibodies that bind to IGF-I or IGF-II and do not cross react with the other. These include references to AF791, AF792, 56408, M23/ILG1-001 and S1F2. Applicant is required to disclose any reference which discusses a combination of any two of the aforementioned antibodies.

The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR 1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained may be accepted as a complete reply to the requirement for that item.

This requirement is an attachment of the enclosed Office action. A complete reply to the enclosed Office action must include a complete reply to this requirement. The time period for reply to this requirement coincides with the time period for reply to the enclosed Office action.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Ben et al, Growth Regulation vol. 1 p. 160 (1991) or Harvey et al Hybridoma vol. 12 p. 737 (1993) or Su et al Hybridoma vol. 16 p. 513 (1997) or Manes et al Endocrinology vol. 138 p. 905 (1997).

Ben et al discloses a monoclonal antibody (sm1.2B) to IGF-I that has partial cross-reactivity to IGF-II (see abstract). For claim 2 this reads on claim 2(a).

Harvey et al discloses monoclonal antibodies 7A1, 1B3 and 5A7 which cross with IGF-I and IGF-II (see Table for cross-reactivity). For claim 2 this reads on claim 2(a).

Su et al disclose monoclonal antibody 35I17 which binds IGF-I and cross-reactis with IGF-II (see p. 515, second column). For claim 2 this reads on claim 2(a).

Manes et al discloses a 2 monoclonal antibodies which react with IGF-I and IGF-II (abstract). For claim 2 this reads on claim 2(a).

The terminology "cancer metastasis inhibitor" in the claims is intended use and does not carry any patentable weight when evaluating compound claims. Furthermore, it is inherent that the antibodies of the references have the ability to inhibit an activity of IGF-I and IGF-II because the antibodies bind IGF-I and II.

Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 03/093317 (published 11/13/03). The English translation of this document is US 2006/0165695.

The WO discloses antibodies and fragments thereof which bind to both hIGF-I and hIGF-II and inhibit their functions (abstract, paragraphs ([0036]-[0052]). These are effective for treating cancer ([0033]).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/513148. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two sets of claims is the scope. Specifically, the antibody in the 148 application has to have a specific binding constant whereas the antibodies in the instant invention includes antibodies with different binding constants. Furthermore, the instant invention reads on any substance whereas the scope in the 148 application is limited to antibodies.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4 are directed to an invention not patentably distinct from claim 1 of commonly assigned 10/513148. Specifically, the reasons have been discussed above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 10/513148, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were

commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claims 1-4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 9-16 of copending Application No. 10/573528. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two sets of claims is the scope. Specifically, the claims in the 528 application not only use a substance/antibody but also require the use of irradiation. Irradiation is a well known treatment for cancer and therefore it would have been obvious to one of ordinary skill in the art to combine the two known cancer treatments with the expected benefits of treating cancer.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 21 and 26-28 of

copending Application No. 10/573378. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two sets of claims is the scope. Specifically, the antibody in the 378 application is limited to a recombinant antibody whereas the in the instant application, the scope is broader in that the substance can be any antibody (polyclonal, monoclonal) and the substance can be any substance. Thus, the scope of the instant application is broader than the 378 application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

With respect the claims 2(b) and 2(c), the Examiner has read these in light of applicants definition on pages 16-17. The terminology "the antibody or the antibody fragment which specifically binds to IGF-I and inhibits the activity of IGF-I" means that the antibody has no cross-reactivity with to IGF-II and "the antibody or the antibody fragment which specifically binds to IGF-II and inhibits the activity of IGF-II" means that the antibody has no cross-reactivity with to IGF-I. In view of this reading, claims 2(b) and 2(c) are free from the art of record. The closest prior art is Enjoh et al J. Biol. Chem vol. 77 p. 510 (1993) and Tamura et al J. Endocrinology vol. 125 p. 327 (1990). Enjoh et al discloses monoclonal antibodies specific for IGF-II that do not cross-react with IGF-I and Tamura et al discloses monoclonal antibodies to IGF-I which do not cross-react with IGF-II. However, reference cannot be combined to obtain a composition

comprising both because each monoclonal antibody is used in an specific assay to detect the specific IGF.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesday and Thursday from 5:30am to 1:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sheela J Huff
Primary Examiner
Art Unit 1643

/Larry R. Helms/

Supervisory Patent Examiner